What is claimed is

~~Claims~~

1. A compound or a derivative thereof, capable of binding to MDM2, particularly human DM2, and specifically inhibiting or blocking the binding of MDM2 to the p53 protein, particularly human p53, *in vitro* or *in vivo*.

2. A compound according to claim 1, wherein the compound is a peptide or derivative thereof.

3. A peptide according to claim 2 which comprises an amino acid motif of the formula

R_1-X-F-X-R_2-R_3-W-X-X-R_4 (I),

wherein

R_1 and is a proline (P), leucine (L), glutamic acid (E), cysteine (C) or glutamine (Q),

X stands for one (any) natural amino acid,

R_2 is arginine (R), histidine (H), glutamic acid, cysteine, serine, or preferably aspartic acid (D),

R_3 is histidine (H), phenylalanine (F) or tyrosine (Y),

R_4 is phenylalanine (F), glutamine (Q) or leucine (L); and

F is phenylalanine and W is tryptophan;

or a derivative of said peptide.

4. A peptide according to claim 3 comprising the amino acid motif of formula (I) consisting of no more than fifteen amino acids (15mers), or a derivative thereof.

5. A peptide according to claim 3 selected from the group consisting of the peptides with the sequences M-P-R-F-M-D-Y-W-E-G-L-N, Q-P-T-F-S-D-Y-W-K-L-L-P, and P-X-F-X-D-Y-W-X-X-L, or a derivative thereof.

6. A derivative of a peptide according to claim 3 which is a fragment comprising at least eight consecutive amino acids of the sequence of formula (I), or a derivative thereof.

7. A fragment according to claim 6, which is an 8mer peptide of formula

$F\text{-}X_2\text{-}R_2\text{-}R_3\text{-}W\text{-}X_3\text{-}X_4\text{-}R_4$ (Ib),

wherein R_2, R_3 and R_4, independently from one another, each have the meanings and preferences given for formula (I),

X_2 is methionine, isoleucine, threonine, arginine, alanine or serine, preferably methionine;

X_3 is glutamic acid, threonine, alanine, phenylalanine or serine, preferably glutamic acid;

X_4 is glycine, glutamine, threonine, alanine or aspartic acid, preferably glycine,

or a derivative of such fragment.

8. A fragment according to claim 6 having the formula

$X_1\text{-}F\text{-}X_2\text{-}R_2\text{-}R_3\text{-}W\text{-}X_3\text{-}X_4\text{-}R_4$ (Ic),

wherein

R_1, R_2, R_3 and R_4, independently from one another, each have the meanings and preferences given for formula (I)

X_1 is arginine, asparagine, alanine, threonine or valine; particularly arginine

X_2 is methionine, isoleucine, threonine, arginine, alanine or serine; preferably methionine;

X_3 is glutamic acid, threonine, alanine, phenylalanine or serine; preferably glutamic acid;

X_4 is glycine, glutamine, threonine, alanine or aspartic acid, preferably glycine,

or a derivative of such fragment.

9. A fragment according to claim 6 selected from the group of fragments consisting of: P-A-F-T-H-Y-W-P, P-T-F-S-D-Y-W-P and P-R-F-M-D-Y-W-P, or a derivative thereof.

10. Use of a compound according to any of claims 1 to 9 for the identification of a molecule binding to MDM2.

11. Use of a compound according to any of claims 1 to 9 for the purification of a binding partner, particularly MDM2.

12. Use of a compound according to any of claims 1 to 9 in a method aiming at identifying or designing compounds which interfere with the binding of MDM2 to p53.

13. Use of a compound according to any of claims 1 to 9 for diagnosis of a disease.

14. A pharmaceutical composition that is suitable for admin istration to a warm-blooded animal, including humans, or to cells or cell lines derivable from a warm-blooded animal, including a human, for the treatment or prevention of a disease that responds to inhibition of the interaction of p53 with MDM2, said composition comprising an amount of a compound according to any of claims 1 to 9, which is effective for said inhibition, together with at least one pharmaceutically acceptable carrier.

15. The use of a compound according to any of claims 1 to 9 for the preparation of a pharmaceutical composition for the treatment or prevention of a disease that responds to inhibition of the interaction of p53 with MDM2.

16. A process for the preparation of a peptide or a derivative thereof according to any of claims 2 to 9 comprising reacting a fragment of such peptide, which has a free carboxy group, or a reactive derivative thereof, with a complementary fragment that has an amino group with at least one free hydrogen atom, or with a reactive derivative thereof, resulting in the formation of a peptide bond, and, if desired, removing a present protecting group, or derivatising said peptide or derivative.

17. A method of treating or preventing a disease comprising administering a therapeutically useful amount of a compound according to any of claims 1 to 9.

18. A method for inducing growth arrest or apoptosis in tumor cells which contain wild type p53 and non-elevated MDM2 levels comprising inhibiting the interaction between MDM2 and p53 *in vivos* or *in vitro*.

19. The method of claim 18 wherein the inhibiting step further comprises interfering with expression of MDM2 by administering antisense oligonucleotides to a cell.

20. The method of claim 19 wherein the inhibiting step further comprises interfering with expression of MDM2 by administering triple strand forming oligonucleotides.

21. The method of claim 19 wherein the inhibiting step further comprises administering to a cell a DNA molecule which expresses a peptide capable of binding to MDM2.

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22. The method of claim 21 wherein the DNA molecule express s a peptide or a derivative thereof according to any of claims 2 to 9.

Sub a4

23. A method of treating or preventing a hyperproliferative disease comprising tumor cells having wild type p53 and a non-elevated MDM2 level, the method comprising interfering with the interaction of human p53 and human MDM2.

add a5